

REPLY

Serial No. 09/808,558

Atty. Docket No. GP068-05.CN3

Amendments to the Claims**The current status of the claims is as follows:**

Claims 1-421 (Canceled)

422. (Currently Amended) ~~An oligonucleotide~~ A hybridization assay probe for use in determining the presence of a nucleic acid analyte in a sample, the probe comprising a detectable label and first and second base regions capable of hybridizing to each other under nucleic acid assay conditions to form a hybrid containing at least one ribonucleotide modified to include a 2'-O-alkyl substitution to the ribofuranosyl moiety, ~~wherein the hybrid is more stable than a hybrid formed between unmodified forms of the first and second base regions, and wherein the oligonucleotide probe forms a stable, double-stranded~~ hybrid with the nucleic acid analyte but not with a non-targeted nucleic acid under nucleic acid assay conditions, such that the nucleic acid analyte can be detected.

423. (Currently Amended) The oligonucleotide probe of claim 422, wherein that portion of the first base region capable of forming a hybrid with the second base region under nucleic acid assay conditions includes a cluster of at least about 4 ribonucleotides modified to include a 2'-O-alkyl substitution to the ribofuranosyl moiety.

424. (Currently Amended) The oligonucleotide probe of claim 422, wherein that portion of the first base region capable of forming a hybrid with the second base region under nucleic acid assay conditions includes at least one nucleotide which is not a ribonucleotide modified to include a 2'-O-alkyl substitution to the ribofuranosyl moiety.

425. (Currently Amended) The oligonucleotide probe of claim 422, wherein each nucleotide of that portion of the first base region capable of forming a hybrid with the second base

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region under nucleic acid assay conditions is a ribonucleotide modified to include a 2'-O-alkyl substitution to the ribofuranosyl moiety.

426. (Currently Amended) The ~~oligonucleotide~~ probe of claim 422, wherein each nucleotide of the ~~oligonucleotide~~ probe is a ribonucleotide modified to include a 2'-O-alkyl substitution to the ribofuranosyl moiety.

427. (Currently Amended) The ~~oligonucleotide~~ probe of claim 422, wherein the ~~oligonucleotide~~ probe includes a conjugate molecule.

428. (Currently Amended) The ~~oligonucleotide~~ probe of claim 423, wherein the ~~oligonucleotide~~ probe includes a conjugate molecule joined to the ~~oligonucleotide~~ probe at a site located within the cluster of the first base region.

429. (Currently Amended) The ~~oligonucleotide~~ probe of claim 422, wherein the ~~first and second base regions are contained within an oligonucleotide that of claim 422, wherein the~~ oligonucleotide is up to about is between 10 and 100 bases in length.

430. (Canceled)

431. (Currently Amended) The ~~oligonucleotide~~ probe of claim ~~430~~ 422, wherein the ~~reporter group label~~ comprises a fluorescent molecule.

432. (Currently Amended) The ~~oligonucleotide~~ probe of claim 422, wherein the nucleic acid analyte comprises RNA.

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433. (Currently Amended) The oligonucleotide probe of claim 432, wherein the nucleic acid analyte comprises ribosomal RNA.

Claims 434-439 (Canceled)

440. (Currently Amended) The oligonucleotide probe of claim 422, wherein the 2'-O-alkyl substitution to the ribofuranosyl moiety is a 2'-O-methyl substitution.

441. (Withdrawn) A method for determining the presence of a nucleic acid analyte in a sample, the method comprising the steps of:

- a) providing to the sample the oligonucleotide probe of claim 422;
- b) incubating the sample under conditions such that the oligonucleotide probe hybridizes to the nucleic acid analyte, if present, to form a probe:analyte duplex; and
- c) determining whether the oligonucleotide has hybridized to the nucleic acid analyte duplex has formed as an indication of the presence of the nucleic acid analyte.

442. (Withdrawn) The method of claim 441, wherein that portion of the first base region capable of forming a hybrid with the second base region under nucleic acid assay conditions includes a cluster of at least about 4 ribonucleotides modified to include a 2'-O-alkyl substitution to the ribofuranosyl moiety.

443. (Withdrawn) The method of claim 441, wherein that portion of the first base region capable of forming a hybrid with the second base region under nucleic acid assay conditions includes at least one nucleotide which is not a ribonucleotide modified to include a 2'-O-alkyl substitution to the ribofuranosyl moiety.

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444. (Withdrawn) The method of claim 441, wherein each nucleotide of that portion of the first base region capable of forming a hybrid with the second base region under nucleic acid assay conditions is a ribonucleotide modified to include a 2'-O-alkyl substitution to the ribofuranosyl moiety.

445. (Withdrawn) The method of claim 441, wherein each nucleotide of the oligonucleotide probe is a ribonucleotide modified to include a 2'-O-alkyl substitution to the ribofuranosyl moiety.

446. (Withdrawn) The method of claim 441, wherein the oligonucleotide probe includes a conjugate molecule.

447. (Withdrawn) The method of claim 442, wherein the oligonucleotide probe includes a conjugate molecule joined to the oligonucleotide probe at a site located within the cluster of the first base region.

448. (Withdrawn) The method of claim 441, wherein the first and second base regions are contained within an oligonucleotide that is between 10 and 100 bases in length.

449. (Canceled)

450. (Withdrawn) The method of claim ~~449~~ 441, wherein the reporter group label comprises a fluorescent molecule.

451. (Withdrawn) The method of claim 441, wherein the nucleic acid analyte comprises RNA.

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452. (Withdrawn) The method of claim 451, wherein the nucleic acid analyte comprises ribosomal RNA.

Claims 453 to 458 (Canceled)

459. (Withdrawn) The method of claim 441 further comprising the step of quantifying the nucleic acid analyte determined to be present in the sample.

460. (Canceled)

461. (Withdrawn) The method of claim 441, wherein step c) is indicative of the presence or absence of at least one microorganism or virus in the sample.

462. (Withdrawn) The method of claim 441 further comprising the step of providing to the sample a nuclease inhibitor other than a polynucleotide modified to include a 2'-O-alkyl substitution to the ribofuranosyl moiety of a ribonucleotide.

463. (Withdrawn) The method of claim 441, wherein the 2'-O-alkyl substitution to the ribofuranosyl moiety is a 2'-O-methyl substitution.

464. (Previously Presented) The ~~oligonucleotide~~ probe of claim 432, wherein a target sequence contained within the nucleic acid analyte includes a double-stranded region.

465. (Withdrawn) The method of claim 451, wherein a target sequence contained within the nucleic acid analyte includes a double-stranded region.

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466. (New) The probe of claim 422, wherein the hybrid formed between the first and second base regions is more stable than a hybrid formed between unmodified forms of the first and second base regions.

467. (New) The probe of claim 466, wherein the 2'-O-alkyl substitution to the ribofuranosyl moiety is a 2'-O-methyl substitution.

468. (New) The probe of claim 423, wherein the 2'-O-alkyl substitution to the ribofuranosyl moiety is a 2'-O-methyl substitution.

469. (New) The probe of claim 424, wherein the 2'-O-alkyl substitution to the ribofuranosyl moiety is a 2'-O-methyl substitution.

470. (New) The probe of claim 425, wherein the 2'-O-alkyl substitution to the ribofuranosyl moiety is a 2'-O-methyl substitution.

471. (New) The probe of claim 426, wherein the 2'-O-alkyl substitution to the ribofuranosyl moiety is a 2'-O-methyl substitution.

472. (New) The probe of claim 429, wherein the 2'-O-alkyl substitution to the ribofuranosyl moiety is a 2'-O-methyl substitution.

473. (New) The method of claim 441, wherein the hybrid formed between the first and second base regions is more stable than a hybrid formed between unmodified forms of the first and second base regions.

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474. (New) The method of claim 473, wherein the 2'-O-alkyl substitution to the ribofuranosyl moiety is a 2'-O-methyl substitution.

475. (New) The method of claim 442, wherein the 2'-O-alkyl substitution to the ribofuranosyl moiety is a 2'-O-methyl substitution.

476. (New) The method of claim 443, wherein the 2'-O-alkyl substitution to the ribofuranosyl moiety is a 2'-O-methyl substitution.

477. (New) The method of claim 444, wherein the 2'-O-alkyl substitution to the ribofuranosyl moiety is a 2'-O-methyl substitution.

478. (New) The method of claim 445, wherein the 2'-O-alkyl substitution to the ribofuranosyl moiety is a 2'-O-methyl substitution.

479. (New) The method of claim 448, wherein the 2'-O-alkyl substitution to the ribofuranosyl moiety is a 2'-O-methyl substitution.